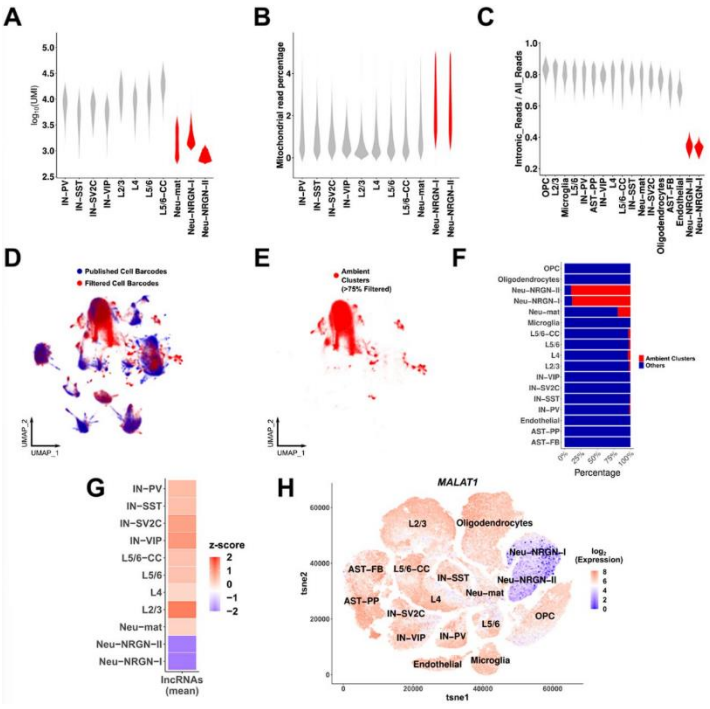
Single Cell Transcriptomics

Newsletter April 2022

Paper 1

Caglayan, E. et al. Ambient RNA analysis reveals misinterpreted and masked cell types in brain single-nuclei datasets-specific neuropathology and multiple neurodevelopmental mechanisms in patient-derived cerebral organoids **bioRxiv (preprint)**, 2022.



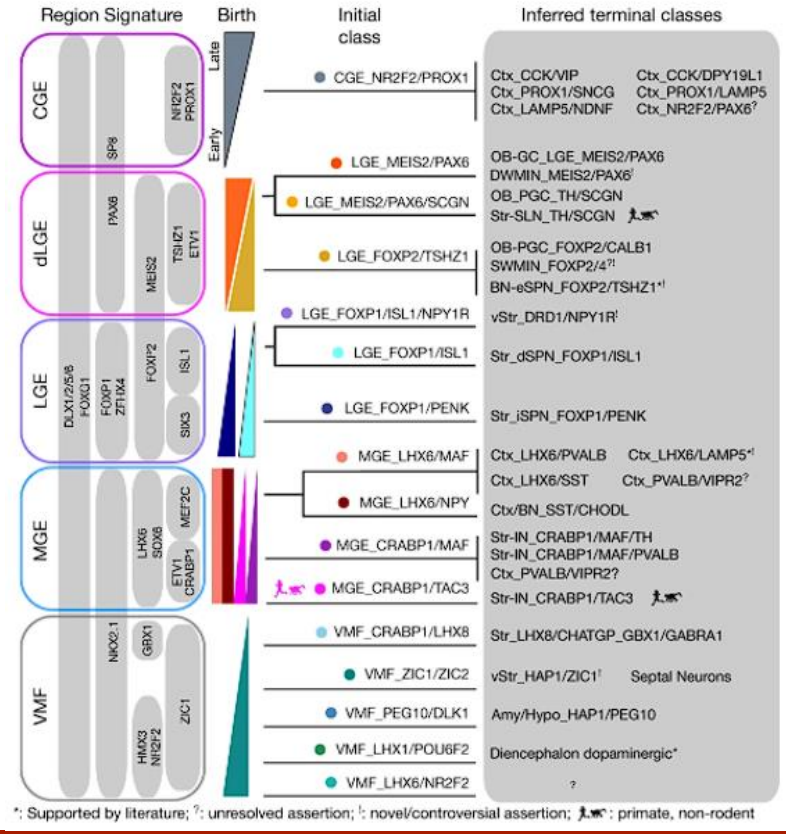
Caglayan *et al.* set out to investigate the effects of ambient RNA contamination on single-cell RNA-seq datasets. They identify cell populations which are most affected by ambient RNA contamination in published brain datasets. Specifically, they found that most ambient RNA came from neuronal sources, which they argued was due to the high abundance of these and their respective axonal processes throughout the brain. Specifically, they found two cell populations, termed Neu-mat and Neu-NRGN which UMIs (unique molecular identifiers) stemmed largely from ambient RNA. These populations were enriched for gene ontology terms such as synaptic development, presynapse, ribosomal subunits and mitochondrial protein. Further, they showed that ambient RNAs in brain is from either nuclear or extra-nuclear origin. Both show predominantly neuronal signatures which contaminate both glial cell populations and give rise to the beforementioned neuronal ambient RNA subtypes. Further by comparing a non-fluorescence-activated nuclear sorted (FANS) brain dataset with a sorted brain dataset, they found that most of the extra-nuclear ambient RNA could be removed from the dataset if nuclei were sorted. Yet, the nuclear ambient RNA was not removed by FANS. To address this problem, they set out remove the ambient nuclear RNA signature *in silico*. By utilizing CellBender, a deep generative model for removal of background-contaminated counts, and enriched ambient genes identified in their analysis they were able to remove nuclear ambient RNA signatures from both glial and neuronal subtypes.

Paper 2

Schmitz, M. et al. The development and evolution of inhibitory neurons in primate cerebrum *Nature, 2022*

The authors of this paper present the gene expression trajectories specifying inhibitory neurons during the neurogenic period in macaques and mice by analyzing 250.181 cells from 71 spatially distinct samples from 9 specimens ranging from postconception day 40 to day 100.

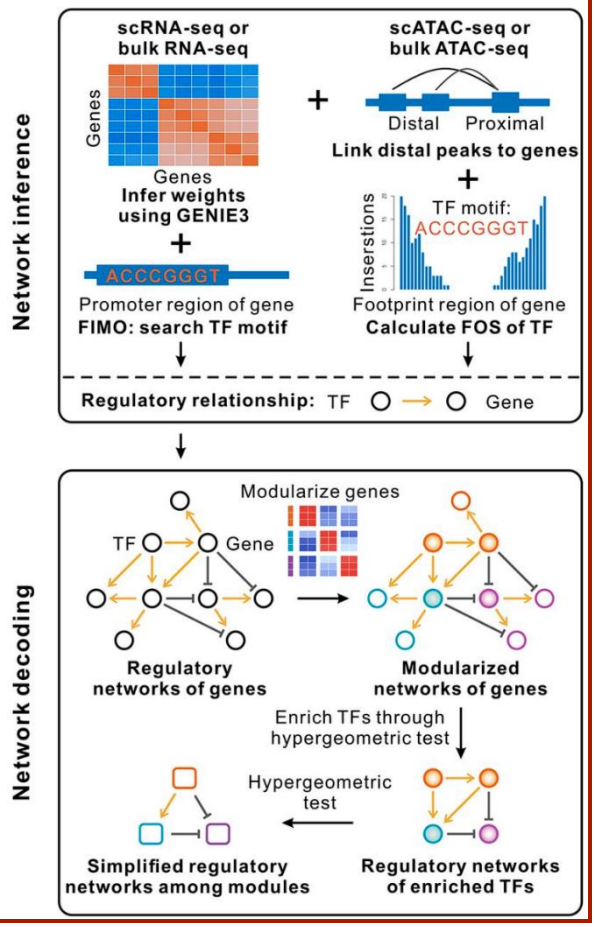
They found that initial classes of inhibitory neurons generated prenatally are largely conserved among mammals. The team presents a taxonomy tree of inhibitory neuron development by identifying evolutionary conserved cell classes and linked them to adult populations. They state that the high conservation of initial classes of inhibitory neurons between mice and macaques suggests that evolutionary diversification of primate inhibitory neurons arises due to radiation of conserved initial classes of new-born neurons and that their cell-fate is ultimately shaped by the expanded diversity of regional destinations the neurons migrate to in the primate brain.



Paper 3

Tyser, R et al. Single-IReNA: integrated regulatory network analysis of single-cell transcriptomes and chromatin accessibility profiles, bioRxiv (preprint), *2022*

In this paper, Tyser et al. presents IReNA (Integrated Regulatory Network Analysis), this method can perform regulatory network analysis by integration of scRNA-seq and scATA-seq data. IReNA consists of two components: Network inference and network decoding. Network inference identifies potential regulatory relationships in scRNA-seq data and links then with transcription factor binding motifs to refine regulatory relationships. Further for scATAC-seq peaks are linked to genes and used to identify transcription factor binding motifs. Network decoding comprises of network modularization, identification of enriched transcription factors and an integrated function to construct simple regulatory networks among modules which are easy to interpret. By testing their method on a publicly available dataset scRNA-seq and scATAC-seq on hepatocytes during liver regeneration the team was able to identify 108 enriched transcription factors. Among the top hits, they found that organic acid catabolism-related gene modules and transcription factors need to be repressed to activate cell cycle progression in hepatocytes and induce liver regeneration. The authors thus demonstrate the power of joint analysis and integration of scRNA-seq and scATAC-seq data for unveiling new regulatory gene networks.



Next Single Cell Seminar

Date: 29th of April 2022,
Location: Zoom, https://ucph-ku.zoom.us/j/66593326709

15:00 – 16:00

Francisco Quintana, Brigham and Women's Hospital, Boston'

Role of astrocytes in the control of CNS inflammation

If you would like to announce anything single cell related, being it job announcement, event, your published paper, technology development etc, please contact us.

Contact: Frederik.sorensen@sund.ku.dk